

PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Docket No: Q92272

Akito YASUHARA, et al.

Appln. No.: 10/562,010

Group Art Unit: 1621

Confirmation No.: 1050

Examiner: Marialouisa LAO

Filed: December 23, 2005

For: 2-AMINO-BICYCLO [3.1.0] HEXANE-2, 6-DICARBOXYLIC ACID DERIVATIVES

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Akito Yasuhara, hereby declare and state:

THAT I am a citizen of JAPAN, residing at Komatsu 4-1-51, Kounosu, Saitama 365-0041, Japan;

THAT I graduated from Setsunan University in 1988 and obtained a doctor's degree from Tohoku University in 1993;

THAT I am employed by Taisho Pharmaceutical Co., Ltd., the Assignee of the above-identified application, where I work in the Pharmaceuticals Laboratory; and

THAT I am one of the co-inventors of the above-identified application and am familiar with the disclosure and the claims of said application.

In order to demonstrate that as compared to the compounds of US Patent No. 5,912,248 the 2-amino-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives of the above-identified

application have superior activity to regulate Group II metabotropic glutamate receptors by introducing a fluorine atom at the 6-position of the bicyclo ring and the Y substituent at 3-position of the bicyclo ring, I conducted the following comparative experimentation.

Experiment

Compound Nos. 10 and 12 described in the specification of the above-identified application were used to compare with the compound of Example 1 in US Patent No. 5,912,248. The compound of Example 1 of US Patent No. 5,912,248 has a similar structure as the structures of Compound Nos. 10 and 12 of the above-identified application, except that the compound of Example 1 in US Patent No. 5,912,248 has hydrogen, not fluorine, at the 6-position of the bicyclo ring and has an X-R substituent at the 4-position of the bicyclo ring instead of the Y substituent at the 3-position of the bicyclo ring. [³H]MGS0008 binding to receptors in CHO cells modified to stably express metabotropic glutamate receptor mGluR2 was measured by the same method as that disclosed in Pharmacological test 2 in the specification of the above-identified application and the concentration (IC₅₀) of each test compound needed to exhibit 50% inhibition was calculated.

The results are shown in the following Table 1. The results show that Compound Nos. 10 and 12 of the above-identified application unexpectedly have binding activities about 20 and 60 times, respectively, as high as the binding activity of the compound of Example 1 of US Patent No. 5,912,248.

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Table I

	Example 1 in US5,912,248	Compound No. 10	Compound No. 12
IC ₅₀	242 nM ^{*1)}	12 nM	3.9 nM

*1) This data is based on the description in US Patent No. 5,912,248.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: October 30, 2007

Akito Yasuhara
Akito Yasuhara